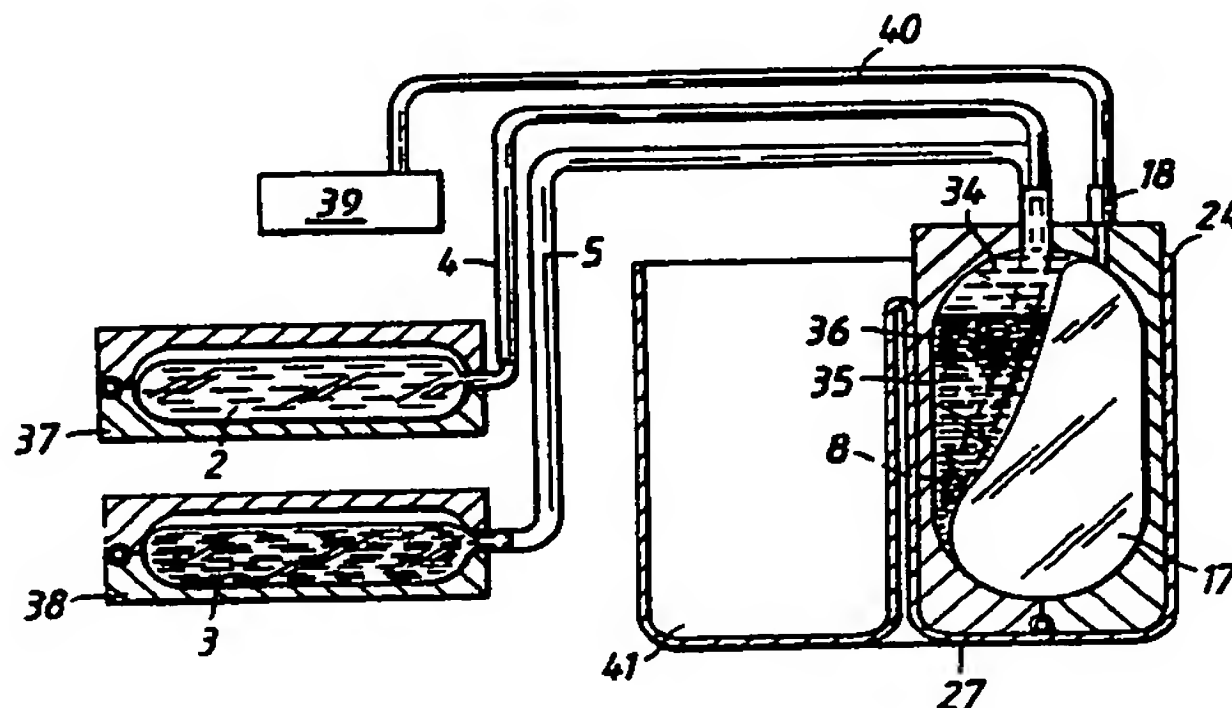




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(21) International Application Number: PCT/SE91/00463 (22) International Filing Date: 26 June 1991 (26.06.91) (30) Priority data: 9002255-9 26 June 1990 (26.06.90) SE (71) Applicant (for all designated States except US): OMEGA TEKNIK HB [SE/SE]; Rödstuguvägen 14, S-181 30 Lid- ingö (SE). (72) Inventors; and (75) Inventors/Applicants (for US only) : UNGER, Peter [SE/ SE]; Värtavägen 35, S-115 29 Stockholm (SE). WEST- BERG, Eric [SE/SE]; Rödstuguvägen 14, S-181 31 Lid- ingö (SE).		(74) Agent: WIEDEMANN, Bernd; AGA Aktiebolag, Patent Department, S-181 81 Lidingö (SE). (81) Designated States: AT (European patent), AU, BE (Euro- pean patent), CA, CH (European patent), DE (Euro- pean patent), DK (European patent), ES (European pa- tent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (Euro- pean patent), NL (European patent), SE (European pa- tent), US. Published <i>With international search report.</i> <i>With amended claims.</i> <i>In English translation (filed in Swedish).</i>

(54) Title: METHOD AND MEANS FOR BLOOD SEPARATION**(57) Abstract**

The present invention relates to a method and to a device for separating blood present in a blood container (1) into components (34, 36, 35) by centrifuging the blood, and for transmitting at least one of three stratified components (34, 35) obtained by centrifugation in sterile fashion to a respective side container (2, 3) connected to the blood container (1) via a respective hose (4, 5). The fluid-actuable displacement body (17) and the blood container (1) are placed in a cassette (12, 13) which, in turn, can be placed in a centrifuge cup (25). The displacement body (17) is in direct abutment with the blood container (1). The displacement body (17) surrounds half the blood container (1) and when fluid is delivered to the body, it will preferably expand, firstly at its lower part and then successively upwards. The cassette (12, 13) is preferably placed in one of two compartments (27) of an intermediate container (24), the other compartment (41) being intended to accommodate the side container (2 and 3 respectively).

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METHOD AND MEANS FOR BLOOD SEPARATION

Conventionally, blood is separated into its various components by collecting blood batches in sterile plastic
5 containers that contain an anticoagulant, to a total volume of about 500 ml, whereafter the containers, together with component containers connected thereto, are lowered into outwardly swingable cups in centrifuges and centrifuged until the blood present in the containers has been stratified in
10 layers of cell concentrate, plasma and an intermediate layer, buffycoat, with a specific weight between the specifically heaviest component, the cell concentrate, and the specifically lightest component, the plasma, to the desired degree of purity. One serious problem with this conventional method
15 resides in transferring the stratified components to the component containers connected to said blood container without slurring or mixing the components.

When practicing conventional methods, the blood containers connected to the component containers are lifted
20 carefully from the cups and placed in presses with the connected component containers positioned free from the press. According to the original method, which is the method most practiced today, the plasma is pressed first into the plasma container, through a hose connected to the top of the
25 blood container, whereafter the buffycoat, when it enters the hose, is passed to a buffycoat container. The cell concentrate remains in the blood container. The drawbacks with this method are that re-slurring of the blood components cannot be avoided when lifting the blood container from the
30 centrifuge cup and placing the container in the press, and that considerable manual work is required in constantly monitoring the transfer process.

According to one alternative method, there is used a blood container which is provided with a bottom connection
35 and which is placed in a press that is provided with a photocell at approximately the level of the buffycoat in the blood container when the blood container is placed in the press, in order to detect the interface between plasma and

CORRECTED

buffycoat. The process of pressing plasma and cell concentrate from the bag into respective component containers is controlled electronically in such a way that upon completion of the transfer process solely buffycoat will remain in the blood container, mixed with some of the other components. Although this method is labor-saving, since it is not necessary to monitor the transfer process, the transfer apparatus is several times as expensive as those normally used and the risk of re-slurrying of the blood components when removing the blood container from the centrifuge cup remains.

According to both methods the blood containers are usually not inserted directly into the centrifuge cups but in an insert therein. Since the blood container must be taken out of the insert this fact does not affect the given description.

One object of the present invention is to provide a method which will prevent re-slurrying of the stratified blood components prior to transferring said components to respective component containers.

Another object of the invention is to provide a cassette which can be used to accommodate the blood container during the process of centrifugation and thereafter to transfer at least one blood component to a component container in a sterile fashion and therewith to avoid re-slurrying.

Still another object of the invention is to provide a method for separating thrombocytes from the buffycoat interlayer obtained subsequent to centrifugation, and to transfer the thrombocytes to a component container intended herefor, in a sterile fashion.

These and other objects of the invention will be apparent from the following description.

The aforementioned drawbacks are alleviated in accordance with the invention in the following manner.

Blood contained in a collapsible container is separated into blood components by centrifugation, wherein, subsequent to the process of centrifugation, at least one of three stratified components is transferred in sterile fashion to a

component container which is connected by means of an open or
penable hose to the upper part of the container, and wherein
the container is placed in a cassette that can be removed
from the centrifuge, together with a fluid-actuable component
5 displacement body which extends along and parallel with one
side of said container.

According to one preferred embodiment, fluid is de-
livered to the displacement body and the displacement body is
constructed such that when fluid is delivered thereto first
10 the lower end of said body will expand, followed by gradual
expansion of the body in an upward direction, thereby
compressing the container first at its lower part and then
successively in an upward direction, wherein the connecti n
between said container and said component container is broken
15 subsequent to having transferred a predetermined quantity of
component, and optionally ceases with the delivery of said
fluid.

According to another preferred embodiment in which the
container is connected to a second component container by
20 means of a second openable hose, the second hose includes a
first extension which extends through a given distance in the
container, taken from an upper container defining surface,
down towards the bottom of the container, wherein, subsequent
to breaking the connection between said container and said
25 component container, the connection to the second component
container is opened while continuing to deliver fluid to the
displacement body, wherein the lower component layer is
transferred to the second component container, and wherein
the delivery of fluid ceases simultaneously or in sequence
30 herewith when a second predetermined quantity of the lower
component layer has been transferred to the second component
container and the connection between the container and the
component container is broken.

According to still another embodiment of the invention,
35 the fluid is removed from the displacement body and a PSM-
solution, i.e. a thrombocyte-suspending medium, is taken from
a third component container and delivered to the intermediate
fraction remaining in the container. This third component

container is connected to the blood container via a third openable hose which opens into the first hose upstream of the connection-breaking location or into the upper end of the container, wherein the container is again centrifuged, this time at a low speed, and fluid is then delivered to the displacement body, so as to transfer an upper layer obtained by said blood centrifugation to the third component container, whereafter the supply of fluid is interrupted and the connection between said container and the third component container is broken.

According to an alternative method, blood is centrifuged in a collapsible container so as to separate the blood into component layers, and, subsequent to centrifugation, at least one of three stratified or layered components is transferred in sterile fashion to a component container which is connected to the upper part of the blood container by means of an open or openable hose, wherein the container is placed in a cassette which can be removed from the centrifuge, together with a fluid-actuable displacement body disposed along and parallel with one side of the blood container, wherein fluid is delivered to the displacement body, which has a construction such that when fluid is delivered thereto, said body will expand first at its lower end and then gradually upwards, such as to compress the container first at its lower end and then successively in an upwards direction; wherein the connection between the container and the component container is broken subsequent to having transferred a predetermined quantity of component to the component container and to the displacement body is optionally ceased with the delivery of fluid. In this case, the hose includes a second extension which extends in the container, towards the bottom thereof, through a second, predetermined distance which is greater than said first predetermined distance, for the transfer of the lower of said three component layers to the cell component container in response to fluid delivery.

When the blood container is connected to a plasma-component container by means of a second openable hose which opens into the upper defining surface of the blood container,

the connection between said blood container and the cell-component container is broken and the connection to the plasma-component container is opened and delivery of fluid to the displacement body is continued. As a result, the upper
5 component, i.e. the plasma, is transferred to the plasma-component container and the delivery of fluid is interrupted when a second predetermined quantity of plasma has been transferred to the plasma container, whereafter the connection between the blood container and the plasma-component
10 container is broken.

Fluid is removed from the displacement body and a PSM-solution is taken from a third component container and added to the intermediate fraction that remains in the blood container, this third component container being connected to
15 the blood container by means of a third openable hose which opens into the second hose upstream of the breaking location or into the upper end of the container, whereafter the blood container is again centrifuged, at a low speed, and fluid is again delivered to the displacement body so as to transfer
20 the upper layer obtained by centrifugation to the third component container, whereafter the delivery of fluid is interrupted and the connection between the blood container and the third component container is broken.

The invention also relates to a device which can be
25 placed in a centrifuge vessel and which functions to transfer, in a sterile fashion, at least one component in a stratified liquid obtained subsequent to centrifuging liquid (blood or blood fraction) present in a collapsible container, to a component container which is connected to the upper part
30 of the blood container by means of an open or openable hose, said device including a container cassette and a fluid-actuable displacement body which is disposed parallel with and along one side of the container and which functions to reduce the container volume when fluid is delivered to said
35 body, thereby effecting transfer of the container content to the component container in open communication with said blood container, wherein the displacement body is in direct abutment with the container, and wherein said device can be

removed from the centrifuge.

The wall of the displacement body preferably has a resistance to expansion which varies in a manner such that displacement of the container contents will take place from the bottom of said container.

It is particularly preferred that the displacement body abuts the container over an area which is essentially equal to half the area of the container, and that the displacement body has a smallest wall thickness at its lower end and that said wall thickness increases with distance from said end.

According to another embodiment of the invention, only that side of the displacement body which faces the container has a varying wall thickness.

According to one embodiment, the displacement body is made of an elastic material of a kind which will return to its original form when no longer influenced by fluid pressure. The displacement body and the blood container may also have a common partition wall.

The blood container is placed in a surrounding, rigid or semi-rigid enclosure, i.e. a cassette, in which it is lowered into an outwardly swingable centrifuge cup and centrifuged, and is not removed from the cassette until the plasma and cell concentrate have been transferred to respective connected component containers. The components are transferred to respective component containers with the aid of an elastic bladder which can be pressurized and abuts, either directly or indirectly, the blood container during the process of centrifugation and component transfer. By pressurizing the bladder subsequent to centrifugation, the blood container is subjected to an overpressure which forces the intended parts of the container content through hoses connected to said container. The plasma is pressed into the plasma container through a connection provided at the top of the blood container. The cell concentrate can be pressed into its component container in a number of different ways. Firstly, the plasma content can be transferred through a hose which is connected internally to the top of the blood container and which extends to a level beneath the buffycoat layer formed

during the process of centrifugation, and secondly, and also preferably, through a hose which is connected internally to the top of the blood container and which has a short length such as to prevent the hose from reaching the buffycoat layer
5 formed during the process of centrifugation.

When practicing the first of these methods, it makes no real difference which of the aforesaid blood components is transferred first to its respective container, or whether the blood components are transferred simultaneously. When
10 practicing the preferred method, however, it is necessary to transfer the plasma first. When the plasma is transferred to its respective container, in accordance with the present invention, the buffycoat layer will rise so that the mouth of the cell-concentrate hose will be located beneath the
15 buffycoat layer. When subsequently the cell concentrate is transferred to its respective container, it will not contain buffycoat. The preferred method has the following advantages over the first mentioned method. The cell concentrate has a greater flow resistance and consequently it is important to
20 use a short transfer hose, and the preferred method uses the shortest hose. In both methods the cell concentrate hose is filled with blood upon commencing the centrifugation process, if not earlier. When practicing the first method, a buffycoat layer is formed in the hoses during the process of centri-
25 fugation, this buffycoat layer subsequently being transferred to the cell-concentrate container and contaminating the cell concentrate. When practicing the preferred method, the blood drains from the hose during the process of centrifugation and is replaced with plasma which is free from buffycoat.

30 In addition to obtaining pure blood components, it is also highly important to be able to separate the largest possible quantities of said blood components in individual containers inexpensively. This can be effected in accordance with the present invention in the following manner, taking
35 int account the particular simplicity of the equipment used. By placing the component containers in volume-limiting cassettes prior to the transfer of said components, the quantity to be transferred can be determined with ut the use

of expensive electronic devices. However, the optimal quantities of the components that can be obtained from a blood unit is determined by the hematocrit of the blood (the cell concentration), which varies from one individual to another. The widest variation, however, depends on the sex of the blood donor, and a good result can be obtained by using separate cassettes for men and women (volumetrically adjustable).

Another advantage afforded by the inventive system is that blood can be drained or tapped at a constant volume without the use of expensive electronic, weight-constant blood-draining cradles. The volume-constant cassette in which the blood is centrifuged can also be used for blood-collecting purposes in combination with a simple rocking device.

The invention will now be described in more detail with reference to exemplifying embodiments thereof illustrated in the accompanying drawings, in which

Figure 1 is a front view of a container unit comprising a blood container provided with a blood-tapping connection and plasma and cell-concentrate containers connected to the blood container by means of hoses;

Figure 2 illustrates a collapsible cassette intended for a blood container and adapted to fit into an intermediate container (into an outwardly swingable centrifuge cup provided with a partition wall), and shows one cassette section provided internally with an elastic bladder that is fitted with a fluid connector;

Figure 3 illustrates the unit shown in Figure 1 with a full blood container in side view and with the container placed in a closed cassette according to Figure 2 and inserted in one of the compartments defined by an inner container equipped with a partition wall and adapted to fit into an outwardly swingable centrifuge cup, wherein the component containers are located in the other compartment;

Figure 4 illustrates the unit shown in Figure 3 subsequent to centrifugation and subsequent to having removed the inner container from the centrifuge cup and connecting the container to a pressure device, with the component containers

placed outside the intermediate container;

Figure 5 illustrates a unit according to Figure 4 during the final stage of a component transfer operation, the blood container being provided with a long extension in the container;

Figure 6 is a front view of a container unit comprising a blood container fitted with a blood-draining connection and hose-connected cell-concentrate, plasma and thrombocyte containers; and

Figure 7 illustrates an intermediate container according to Figures 2-4, in which each compartment is divided into two subcompartments in which two blood bags are centrifuged simultaneously for thrombocyte separation.

Figure 1 illustrates a container unit comprising a blood container 1 which contains an anticoagulant and which is connected to a blood-tapping needle 7 by means of a hose 11. The blood container 1 is also connected by means of a top-connected hose 4 to a plasma-component container 2, the hose 4 being closed at a location adjacent the container 1 by means of an openable closure device 10, for example a shear pin. The upper part of the blood container 1 is connected to a cell-concentrate container 3 by means of a hose 5, said container containing a nutrient solution. The hose 5 includes an extension part 8 which extends into the blood container 1 and which has a side opening 9. The extension part 8 is preferably fairly rigid, although it may also consist of a thin, pliable material. The opening 9 may also be disposed in the longitudinal direction of the extension 8. The hose 5 is fitted with an openable closure device 6 adjacent the container 3, for example a shear pin similar to the closure device 10.

In Figure 2, the reference numerals 12 and 13 identify two cassette halves which are hinged together, e.g., by a hinge 16. The cassette half 13 is lined internally with an expandable displacement body 17, for instance a rubber bladder, which is provided with a fluid connector 18 in the upper part of the cassette holder 13. When assembled, the cassette halves define an inner space 14 + 15 which cor-

responds to a filled blood container 1 both in configuration and volume. The halves are locked together by means of a locking bar or strap 20 which engages a pin or stud 21. Provided in the upper defining surface of the cassette halves 5 12, 13 is an aperture 19 which accommodates the hoses connecting the blood container to the side containers, and optionally also other hoses.

Figure 3 illustrates the unit shown in Figure 1 with the blood container 1 filled with a predetermined quantity of 10 blood 33 and placed in the cassette 12, 13. The needle 7 has been welded-off and the end of the hose 11 (not shown) remote from the blood container has been closed. The cassette 12, 13 is placed in an intermediate container 24, which in turn is placed in a centrifuge cup 25. The centrifuge cup 25 is 15 divided into two compartments 27, 28 by a partition wall 26. The intermediate container 24 has three compartments 29, 30, 31, wherein the shape and size of the cassette 12, 13 corresponds to the shape and size of the compartment 29 and the cassette is placed in this container compartment and 20 located in the compartment 27 of the centrifuge cup. The compartments 30 and 31 of the intermediate containers are disposed in the compartment 28 of the centrifuge cup and are mutually separated by an intermediate wall 32. The plasma container is located in compartment 31 and the cell-con- 25 centrate container, containing said nutrient solution, is placed in compartment 30. The hoses connecting the blood container to respective side containers extend through the aperture 19 provided in the cassette 12, 13. The unit illustrated in Figure 3 is now ready for centrifugation, 30 although has not yet undergone centrifugation.

Figure 4 illustrates the intermediate container 24 with its contents subsequent to having been removed from the centrifuge body 25, upon completion of the centrifugation process. The blood 33 has been divided by centrifugation into 35 plasma 34, cell concentrate 35 and buffycoat 36. The side containers, or component containers 2, 3 that are intended for plasma and blood concentrate have been placed in separate respective compartments 37 and 38. A fluid source, for

instance an air source, is connected to the connector 18 of the displacement body 17 by means of a hose 40. In this embodiment, the intermediate container 24 has only two compartments, i.e. compartment 29 for the cassette 12, 13 and compartment 41 for the component containers 2, 3. The source of fluid 39 may be an air compressor or a container for pressurized gas.

Figure 5 illustrates the same arrangement or unit as that shown in Figure 4, but with the exception that fluid has been delivered to the displacement body 17, such that the component holder 2 is filled with plasma and the component holder 3 is almost filled with cell concentrate. When fluid is delivered to the displacement body 17, the body first expands at its lower part and then continues to expand successively upwards. The intermediate layer 36, buffycoat and residues of plasma and cell concentrate, remain in the blood bag. The displacement body 17 is made of an elastic material, preferably a material which will return to its original shape and form when the fluid has been removed from the body. The body also has a thinnest wall thickness at its lower part, with the wall thickness of said body gradually increasing in value. Alternatively, the body 17 may be provided with parallel, transversely extending thinner parts which are disposed more densely in the lower part of the body and more sparsely in the upper part thereof. The displacement body 17 preferably encloses half the filled blood container 1 in the cassette 12, 13, optionally with the exception of the uppermost part of said container 1.

Figure 6 illustrates a container unit 42 which includes the container unit shown in Figure 1. The container unit 42 includes a thrombocyte container 43 which includes a thrombocyte-suspending medium. The container 43 is connected, by means of a hose 47, to a branch tube 44 mounted in the hose extending between the blood container and the plasma component container 2. In the case of this embodiment, the plasma container 2 is connected by means of a hose 45 to the branch tube 44, and the hose 5 is connected to the third outlet of the branch 2. An openable closure device is mounted

in the hose 47 at a location adjacent the upper defining surface of the container 43. This closure device may be of the same kind as the closure devices 6 and 10 of the Figure 1 embodiment. The hose 11 by means of which blood is delivered to the container 1 is not shown. All hoses 4, 5, 11, 45 and 47 are made of a pliable material.

Figure 7 illustrates an intermediate container 50 inserted in the centrifuge cup 25. The intermediate container 50 has two compartments 51, 52, each of which is divided into two subcompartments 55, 56 and 57, 58 respectively by means of two partition walls 53, 54. Arranged in each subcompartment 55, 56 of the compartment 51 is a respective displacement body 61 and 62 and a respective buffycoat-containing blood bag 1' and 1". A thrombocyte-component container 63, 64 is arranged in respective subcompartments 57, 58 of the compartment 52. The blood bag 1' is connected to the thrombocyte container 64 by means of a hose 66, while the blood bag 1" is connected to the thrombocyte container 63 by means of hose 65. The displacement bodies 61, 62 are connected to a fluid source by means of a hose 67. The Figure illustrates the arrangement subsequent to completing a second centrifuging process at a lower speed than the first centrifuging process, and with the component containers for plasma and cell concentrate removed.

A unit of blood is drained or tapped into the blood container 1 in a conventional manner, said container containing a predetermined quantity of anticoagulant, whereafter the blood-tapping needle 7 is welded-off. The component container 3 for cell concentrate contains a predetermined quantity of nutrient solution. The blood container 1 is then placed in the cassette 12, 13, provided with the displacement body 17, and the cassette is closed and lowered into one compartment 29 of the intermediate container 24. The component containers 2 and 3 are placed, together with their connecting hoses, into two respective second compartments 31 and 30 in the intermediate container. The intermediate container 24, together with its contents, is then placed in the outwardly swingable centrifuge cup 25 of a centrifuge and

then centrifuged. In order to achieve rapid and more effective separation of the blood components, it is beneficial to suspend the centrifuge cup eccentrically in the centrifuge, so that during a working revolution of the centrifuge, the centrifuge cup will form an angle of from 30 to 45 degrees with the vertical. Alternatively, the cassette 12, 13 can be constructed so that the blood bag will define the aforesaid angle during centrifugation. The blood 33 present in the blood container 1 is therewith divided into the components plasma 34, cell concentrate 35 and an intermediate buffycoat 36. The extension 8 shown in Figures 1, 3 and 4 and extending down in the container 1 is so short that its laterally directed orifice 9 will now be located in the plasma space.

When taking blood from a blood donor, the hose extension 8 will become partially filled with blood, but when the buffycoat layer is formed during the process of centrifugation, this blood will be caused to run from the extension, by the forces of centrifugation, and will be replaced with plasma. In order to utilize the centrifuge effectively, the intermediate container, with the cassette 12, 13 and component containers 2, 3, is lifted from the centrifuge body 25 and placed on a flat surface. A pressure source, for instance a compressed air source 39, is connected to the fluid connection 18 of the displacement body 17. The closure device 10 provided for opening the connection to the plasma container 2 is opened and fluid is then delivered to the displacement body 17. The displacement body 17 is so constructed, through its varying wall thickness, that said body will first compress the lower part of the blood container 1, the displacement body 17 being expanded from the bottom and upwards, as indicated in Figure 5. The container 1 is emptied so that the upper layer 34 (Figure 4), i.e. the plasma, flows into the plasma container 2. Subsequent to transferring a predetermined quantity of plasma, i.e. when the plasma container is full, the closure device 10 of the cell concentrate container 3 is opened, this container containing nutrient solution for the blood cells. As the plasma is displaced upwards in the container 1, the buffycoat layer 36

will pass the orifice 9 in the extension line 8. As the closure device is opened, any connection to the plasma container is closed, e.g. with the aid of a hose clamp. When switching from plasma to cell concentrate, the delivery of fluid may be interrupted temporarily. When delivery of said fluid is continued, cell concentrate, which is now located around the orifice 9 of the extension 8, will flow over into the container 3. Subsequent to having transferred said predetermined quantity of cell concentrate and the concentrate container is full, the delivery of fluid is interrupted and the connection between the containers 1 and 3 is broken. The component containers 2 and 3 are then removed from the intermediate container 24 and the hoses 4 and 5 are welded-off and sealed permanently. The cassette containing the blood container 1, which now contains solely buffycoat and residues of plasma and cell concentrate, is removed from the cassette for subsequent separation of thrombocytes. The afore described procedure can also be carried out in the centrifuge cup, although with the disadvantage that in that case the centrifuge cannot be used during the transfer.

According to one alternative method, the intermediate container 24 is removed from the centrifuge cup 25 upon completion of the centrifugation process and placed on a supporting surface. Instead of being left in the intermediate container 24, the component containers are removed and placed into separate compartments, as shown in Figures 4 and 5.

The embodiment illustrated in Figure 5 differs from the embodiments shown in Figures 2, 3 and 4, in that the blood bag has an extension 70 which extends far into the blood container 1, at least to a location beneath the buffycoat layer 36 formed upon centrifugation. The transfer of the blood-components plasma and cell concentrate can therewith be effected in the same order or in the reverse order, or even at one and the same time.

The container unit 42 illustrated in Figure 6 is used when thrombocytes are separated from buffyc at in conjunction with transferring plasma and cell concentrate to their respective containers 2, 3. Upon completion of the plasma and

cell-concentrate transfer, the hose 45, which connects the plasma container with the branch pipe 44, is welded-off instead of the hose 5. The thrombocyte-suspending medium, the PSM-solution, in the container 43 is delivered to the blood container 1, and the blood container 1 is placed in the intermediate container 50, in accordance with Figure 7. In the case of the illustrated embodiment, two blood containers 1 can be placed in respective subcompartments 55, 56, whereas the associated component containers 43 are placed in respective subcompartments 57 and 58. A further centrifugation process is carried out subsequent to having placed the intermediate container in the centrifuge body 24, although this time at a lower speed than that at which the first centrifugation process was carried out. By lower speed is meant in the present description and claims that the blood container is subjected to less g-forces to which the container is subjected. Subsequent to centrifugation, a displacement sequence similar to that described with reference to Figures 3 and 4 in the case of plasma displacement takes place.

CLAIMS

1. A method of separating blood into components by centrifuging blood present in a collapsible container, comprising the steps of transferring in sterile fashion at least one of
5 three components stratified by said centrifugation process to a side container connected to the upper part of the blood container by means of an open or openable hose, characterized by the further step of placing the container in a cassette that can be removed from the centrifuge, together with a
10 fluid-actuable displacement body arranged along and parallel with one side of the container.
2. A method according to Claim 1, characterized by delivering fluid to said displacement body, said body having a construction such that when fluid is delivered thereto, said
15 body will expand first at its lower end and then gradually upwards, whereby the container is compressed first at its lower part and such that said compression will propagate in an upward direction; breaking the connection between the blood container and the side container when a predetermined
20 quantity of component has been transferred to said side container; and optionally stopping the fluid delivery.
3. A method according to Claim 2, in which the blood container is connected to a second side container by means of a second openable hose, wherein the second hose includes an
25 extension part which extends towards the container bottom through a predetermined distance, taken from the upper defining surface of said container, wherein the orifice of said extension part is located above the center layer of said three layers subsequent to centrifugation, characterized by
30 the further steps of opening the connection to the second side container subsequent to breaking the connection between said container and the first side container; continuing to deliver fluid to the displacement body, such as to transfer the lower component to the second side container; interrupting the delivery of fluid, simultaneously or in sequence,
35 when a second predetermined quantity of the lower component has been transferred to the second side container; and breaking the connection between the blood container and the

side container.

4. A method according to Claim 3, characterized by removing the fluid from the displacement body; adding a PSM-solution, i.e. a thrombocyte-suspending medium, to the remaining
5 intermediate fraction in said container, said PSM-solution being taken from a third side container which is connected to said container by means of a third openable hose which opens into the first hose upstream of the location at which said connection is broken, or opens into the upper end of said
10 container; centrifuging the container again, at a low speed; delivering fluid to the displacement body such as to transfer the upper layer obtained by centrifugation to the third side container; interrupting the delivery of fluid; and breaking the connection between the container and the third side
15 container.

5. A method according to Claim 1, in which the container is connected to a second side container by means of a second openable hose which includes an extension hose which extends into the container towards the bottom thereof through a first
20 predetermined distance, taken from the upper defining surface of said container, wherein the orifice of said extension hose is located beneath the center layer of the three layers subsequent to centrifugation, characterized by optionally opening the hoses to both side containers and delivering
25 fluid to the displacement body, said displacement body having a construction such that when fluid is delivered thereto, said body will expand first at its lower end and thereafter gradually upwards, such as to compress the container first at its lower end and then successively upwards, thereby filling
30 both side containers simultaneously; and by breaking the connection between the container and respective side containers when a predetermined quantity of the component has been transferred to the side container, whereafter the delivery of fluid is interrupted.

35 6. A method according to Claim 2, in which the container is connected to a second side container by means of a second openable hose which includes an extension hose and which extends into the container, towards the bottom thereof,

through a first predetermined distance, taken from the upper defining surface of said container, the orifice of said extension hose being located beneath the center layer of the three layers subsequent to centrifugation, characterized by
5 transferring the lower of the three components to the side container in response to said fluid delivery.

7. A method according to Claim 2, in which the container is connected to a second side container by means of a second openable hose which includes an extension hose that extends
10 in the container, towards the bottom thereof through a first predetermined distance, the orifice of said extension hose being located beneath the centermost of the three layers subsequent to centrifugation, characterized by opening the connection to the second side container; continuing to
15 deliver fluid to the displacement body, such as to transfer the upper component to the second side container; simultaneously or in sequence herewith, interrupting the delivery of fluid when a second predetermined quantity of the upper component has been transferred to the second side container;
20 and breaking the connection between the blood container and the side container.

8. A method according to Claim 3, characterized by removing the fluid from the displacement body and adding to the intermediate fraction remaining in the container a PSM-
25 solution taken from a third side container which is connected to the blood container by means of a third openable hose which opens into the second hose upstream of the connection-breaking location or into the upper end of the blood container; again centrifuging the container, at a low speed;
30 delivering fluid to the displacement body, to transfer to the third side container an upper component layer obtained by centrifugation; interrupting the delivery of fluid; and breaking the connection between the blood container and the third side container.

35 9. A method according to Claim 1, characterized by causing the longitudinal axis of the blood container to define an angle f between 30 and 45 degrees with the vertical during the centrifugation process at stationary speed.

10. A device which can be placed in a centrifuge vessel for the sterile transfer of at least one component of a stratified liquid obtained subsequent to centrifuging a liquid (blood or blood fraction) present in a collapsible container to a side container connected to the upper part of the blood container by means of an open or openable hose, said device including a container cassette and a fluid-actuable displacement body which is arranged parallel with and along one side of the blood container and which when fluid is delivered thereto functions to reduce the volume of said container, thereby effecting transfer of the blood in the blood container to the side container in open communication therewith, characterized in that the displacement body is in direct abutment with the blood container; and in that the device can be removed from the centrifuge.

11. A device according to Claim 10, characterized in that the resistance of the wall of the displacement body to expansion varies in a manner such that displacement of the blood container contents begins from the bottom of said container.

12. A device according to Claim 10 or 11, characterized in that the area over which the displacement body abuts the blood container is substantially equal to half the area of said container.

13. A device according to one more of Claims 10-12, characterized in that the displacement body has a thinnest wall thickness at its lower end and in that said wall thickness increases with distance from said end.

14. A device according to one or more of Claims 10-13, characterized in that only the side of the displacement body that faces the blood container has a varying wall thickness.

15. A device according to one or more of Claims 10-14, characterized in that the displacement body is made of an elastic material of a kind which will return to its original form when no longer influenced by fluid pressure.

16. A device according to one or more of Claims 10-15, characterized in that the displacement body and the blood container have a common defining wall.

AMENDED CLAIMS

[received by the International Bureau on 22 November 1991 (22.11.91);
original claims 1-16 replaced by amended claims 1-14 (5 pages)]

1. A method of separating blood into components by centrifuging blood present in a collapsible container, and in sterile fashion transferring at least two of three components stratified by said centrifugation process to separate side containers connected to the upper part of the blood container by means of a first open or openable hose and a second openable hose, respectively, wherein the second hose includes an extension part which extends towards the container bottom through a predetermined distance, taken from the upper defining surface of said container, wherein the orifice of said extension part is located either above or below the center layer of said three layers subsequent to centrifugation and breaking the connection between the blood container and the side containers subsequent to the transfer of the blood component to the respective side container, characterized by the steps of

placing, before centrifugation, the blood container and a fluid actuable displacement body in a cassette enclosing said container and displacement body and having an opening for a fluid connection to the displacement body and the hoses connecting the blood container with the side containers, said displacement body being arranged in direct contact with the container, along and parallel with one side thereof;

actuating, after centrifugation, the displacement body with a fluid in order to transfer the first component to the first side container, in case of an openable hose, after opening the connection between the container and the side container;

opening the connection between the blood container and the second side container subsequent to the completion of the transfer of the first component;

continuing the delivery of fluid to the displacement body such as to transfer the lower component to the second side container;

interrupting the delivery of fluid when a second predetermined quantity of the lower component has been transferred to the second side container.

2. A method according to Claim 1, characterized in that said displacement body is given such a construction that, when fluid is delivered thereto, said body will expand first at its lower end and then gradually upwards, whereby the
5 container is compressed first at its lower part and such that said compression will propagate in an upward direction.

3. A method according to Claim 2, characterized by removing the fluid from the displacement body; adding a PSM-solution, i.e. a thrombocyte-suspending medium, to the remaining
10 intermediate fraction in said container, said PSM-solution being taken from a third side container which is connected to said container by means of a third openable hose which opens into the first hose upstream of the location at which said connection is broken, or opens into the upper end of said
15 container; centrifuging the container again, at a low speed; delivering fluid to the displacement body such as to transfer the upper layer obtained by centrifugation to the third side container; interrupting the delivery of fluid; and breaking the connection between the container and the third side
20 container.

4. A method of separating blood into components by centrifuging blood present in a collapsible container, and in sterile fashion transferring at least two of three components stratified by said centrifugation process to separate side
25 containers connected to the upper part of the blood container by means of a first open or openable hose and a second openable hose, respectively, wherein the second hose includes an extension part which extends towards the container bottom through a predetermined distance, taken from the upper defining surface of said container, wherein the orifice of said
30 extension part is located below the center layer of said three layers subsequent to centrifugation and breaking the connection between the blood container and the side containers subsequent to the transfer of the blood component to the
35 respective side container, characterized by the steps of

placing, before centrifugation, the blood container and a fluid actuable displacement body in a cassette enclosing said container and displacement body and having an opening

for a fluid connection to the displacement body and the hoses connecting the blood container with the side containers, said displacement body being arranged in direct contact with the container, along and parallel with one side thereof;

5 opening, after centrifugation, the second connection and in case of an open first hose closing the first connection and actuating the displacement body with a fluid in order to transfer the heavier component to the second side container;

10 opening the connection between the blood container and the first side container subsequent to the completion of the transfer of the heavier component;

continuing the delivery of fluid to the displacement body such as to transfer the lighter component to the first side container;

15 interrupting the delivery of fluid when a second predetermined quantity of the lighter component has been transferred to the second side container.

5. A method according to Claim 1, characterized in that said displacement body is given such a construction that, 20 when fluid is delivered thereto, said body will expand first at its lower end and then gradually upwards, whereby the container is compressed first at its lower part and such that said compression will propagate in an upward direction.

6. A method according to Claim 2, characterized by removing 25 the fluid from the displacement body; adding a PSM-solution, i.e. a thrombocyte-suspending medium, to the remaining intermediate fraction in said container, said PSM-solution being taken from a third side container which is connected to said container by means of a third openable hose which opens 30 into the first hose upstream of the location at which said connection is broken, or opens into the upper end of said container; centrifuging the container again, at a low speed; delivering fluid to the displacement body such as to transfer the upper layer obtained by centrifugation to the third side 35 container; interrupting the delivery of fluid; and breaking the connection between the container and the third side container.

7. A method of separating blood into components by centri-

fuging blood present in a collapsible container, and in sterile fashion transferring at least two of three components stratified by said centrifugation process to separate side containers connected to the upper part of the blood container by means of a first open or openable hose and a second openable hose, respectively, wherein the second hose includes an extension part which extends towards the container bottom through a predetermined distance, taken from the upper defining surface of said container, wherein the orifice of said extension part is located below the center layer of said three layers subsequent to centrifugation and breaking the connection between the blood container and the side containers subsequent to the transfer of the blood component to the respective side container, characterized by the steps of

15 placing, before centrifugation, the blood container and a fluid actuatable displacement body in a cassette enclosing said container and displacement body and having an opening for a fluid connection to the displacement body and the hoses connecting the blood container with the side containers, said displacement body being arranged in direct contact with the container, along and parallel with one side thereof;

opening, after centrifugation, the second connection and in case of an openable first hose also the first connection and actuating the displacement body with a fluid in order to

25 simultaneously transfer the heavier and lighter component to the respective side container.

8. A device which can be placed in a centrifuge vessel for centrifugation and thereafter sterile transfer of at least two components of a stratified liquid obtained subsequent to centrifuging a liquid (blood or blood fraction) present in a collapsible container to side containers connected to the upper part of the collapsible container by means of hoses, characterized in that said device includes a rigid or semi-rigid container cassette enclosing said container and a

35 fluid-actuatable displacement body being arranged in direct abutment, parallel with and along one side of the container, said cassette having an opening for connections to the displacement body and the container with its side containers,

in that one of the connections of the collapsible container includes an extension part which extends towards the container bottom through a predetermined distance, taken from the upper defining surface of said container, and in that the
5 device can be removed from the centrifuge before the transfer of the components from the container.

9. A device according to Claim 8, characterized in that the area over which the displacement body abuts the blood container is substantially equal to half the area of said
10 container.

10. A device according to Claim 8 or 9, characterized in that the resistance of the wall of the displacement body to expansion varies in a manner such that displacement of the blood container contents begins from the bottom of said
15 container.

11. A device according to one more of Claims 8-10, characterized in that the displacement body has a thinnest wall thickness at its lower end and in that said wall thickness increases with distance from said end.

20 12. A device according to one or more of Claims 8-11, characterized in that only the side of the displacement body that faces the blood container has a varying wall thickness.

13. A device according to one or more of Claims 8-12, characterized in that the displacement body is made of an
25 elastic material of a kind which will return to its original form when no longer influenced by fluid pressure.

14. A device according to one or more of Claims 8-13, characterized in that the displacement body and the container have a common defining wall.

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Fig. 1

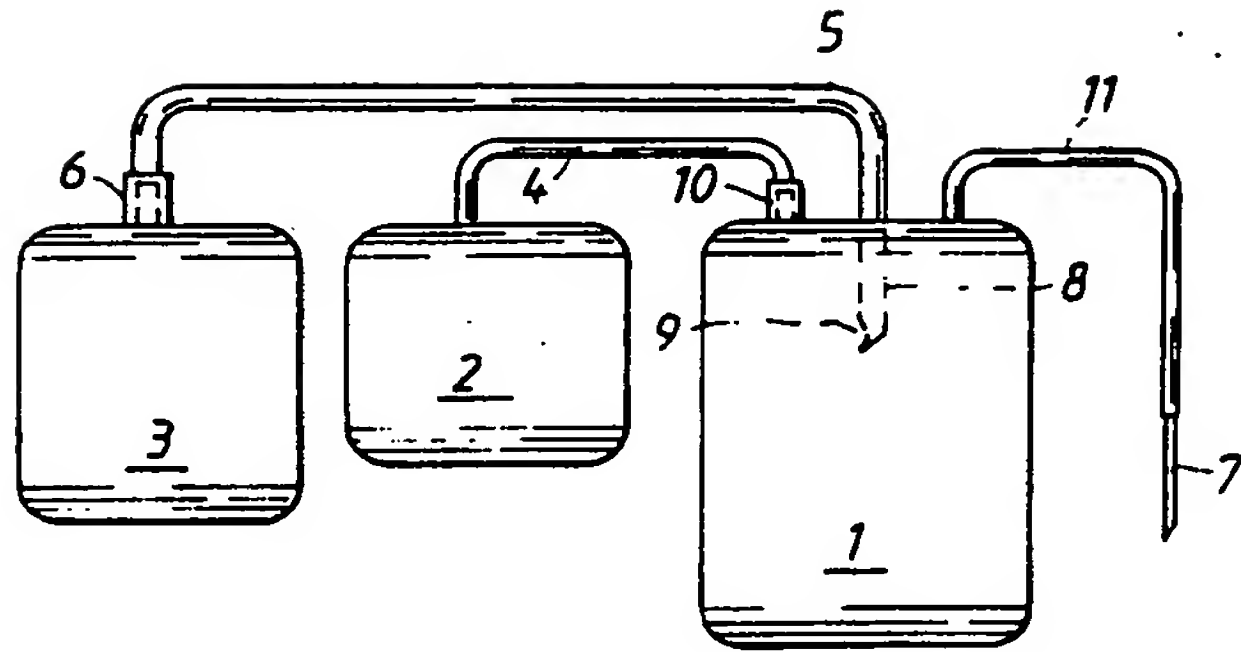


Fig. 2

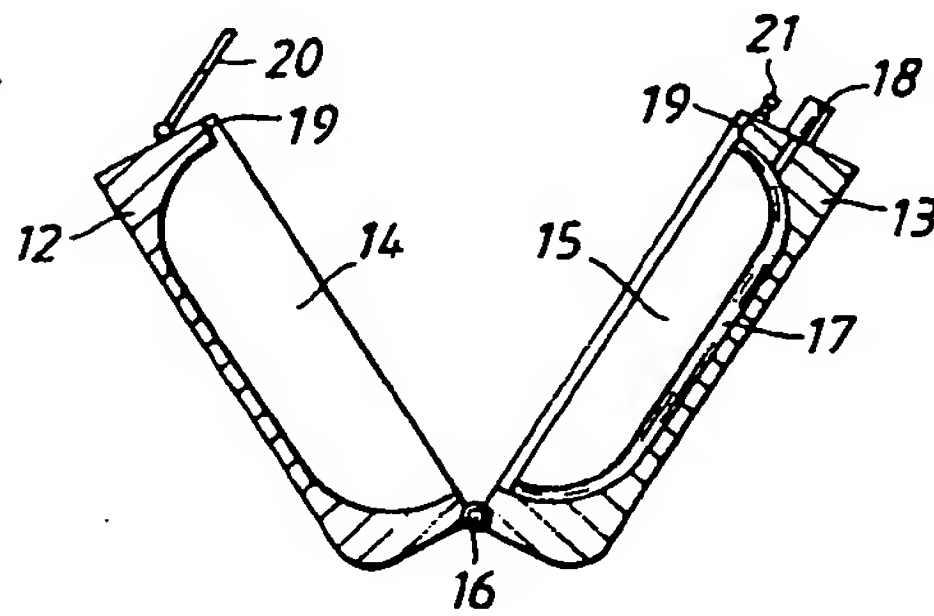


Fig. 3

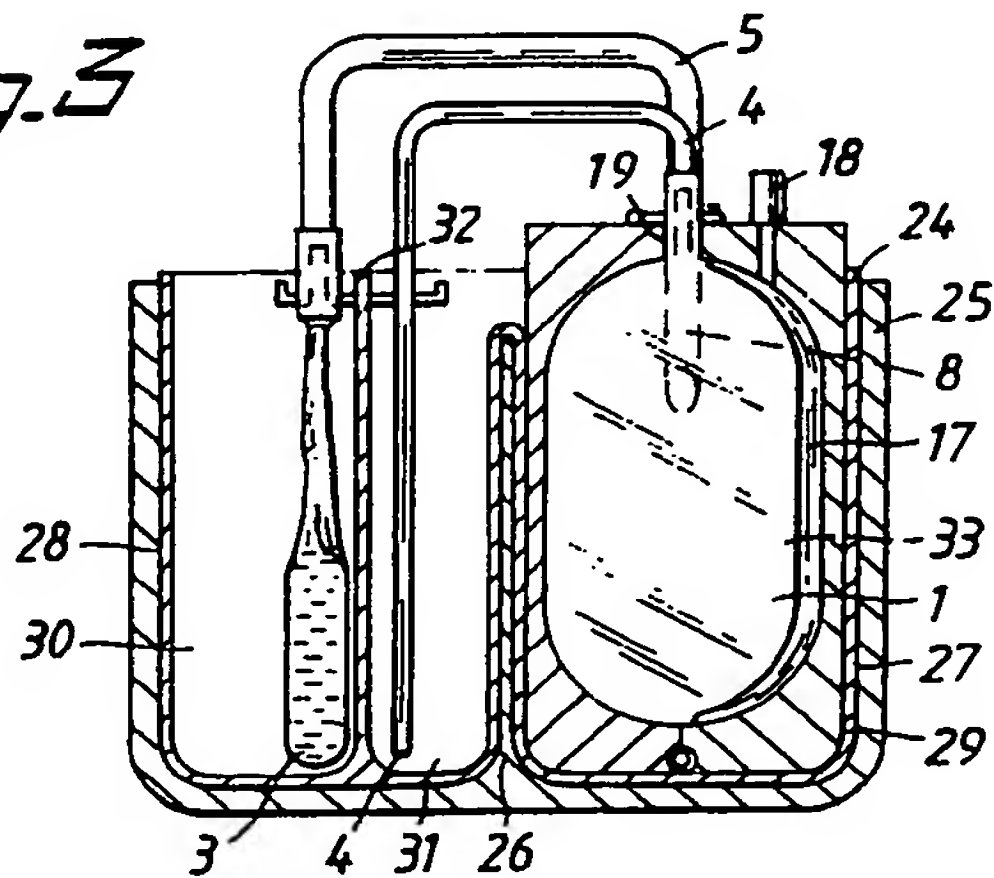


Fig. 4

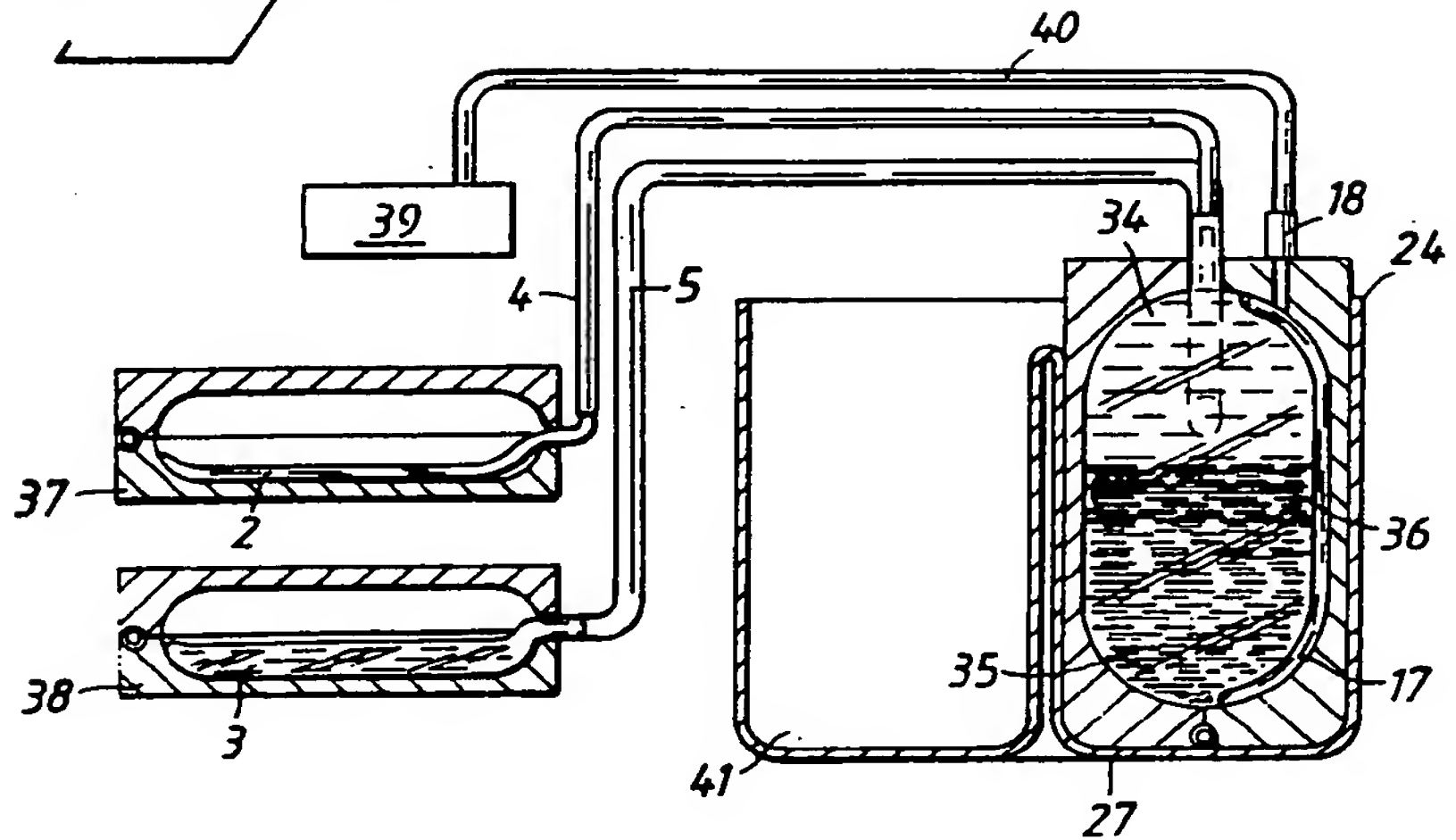
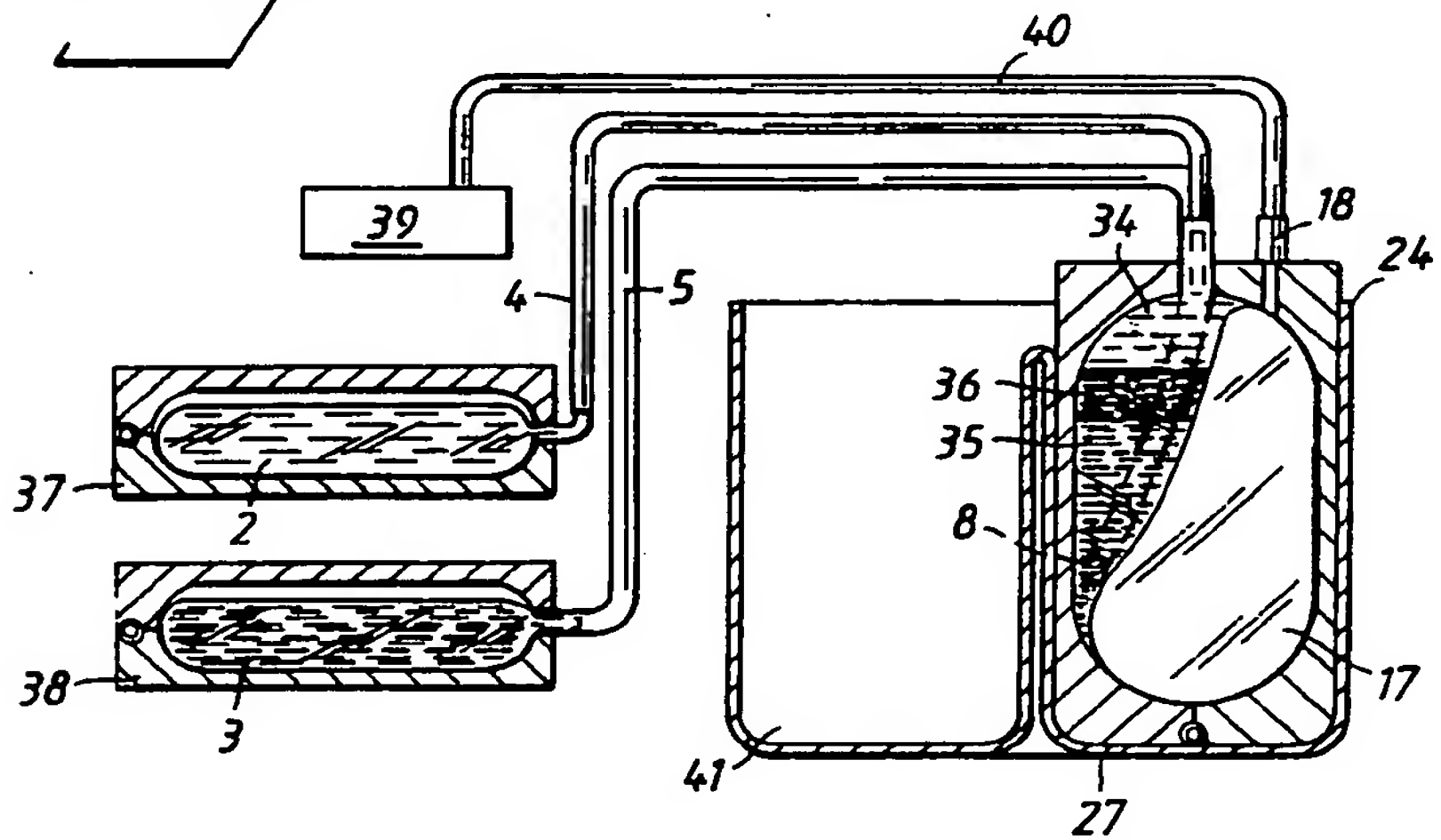


Fig. 5



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Fig. 6

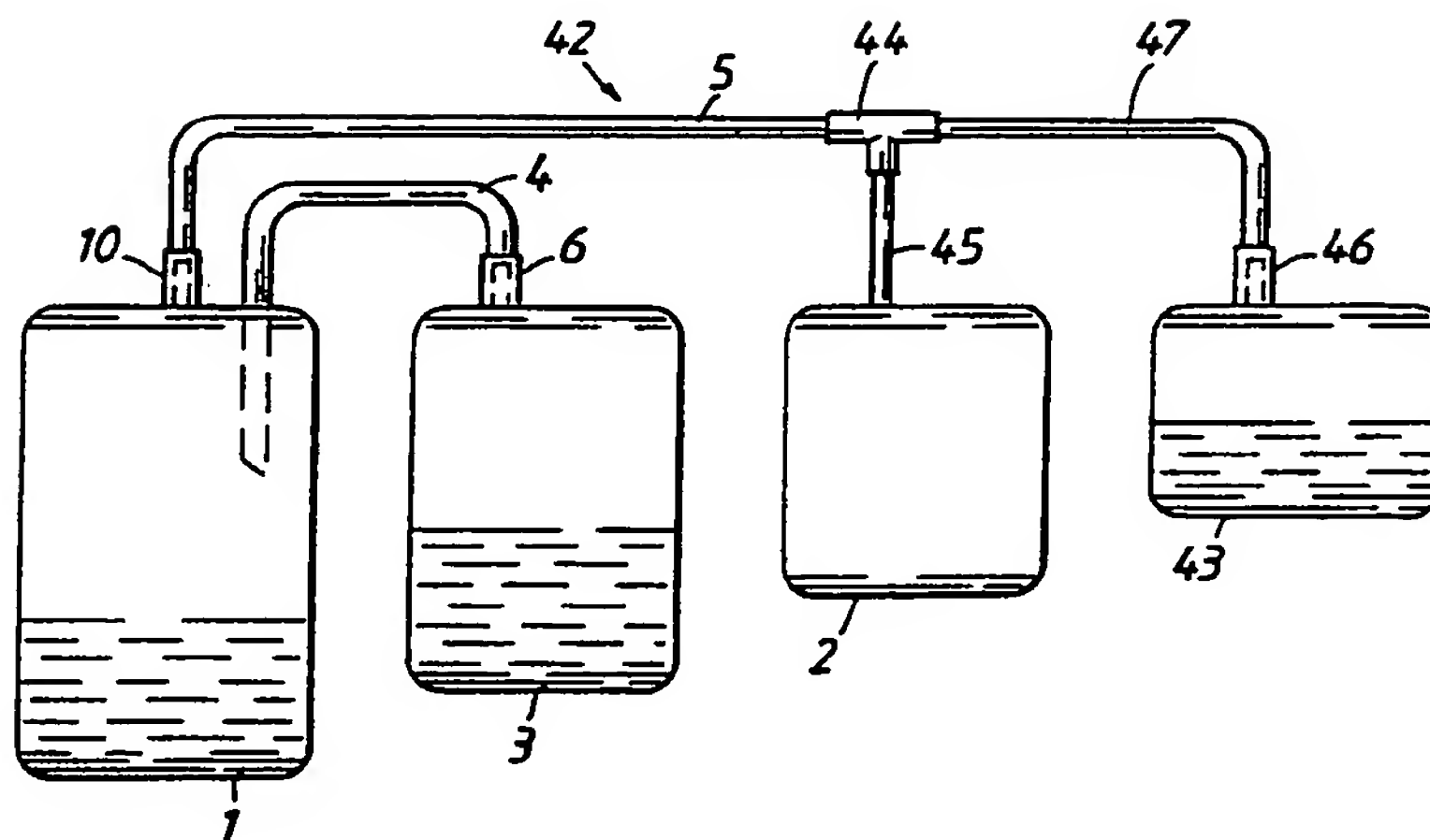
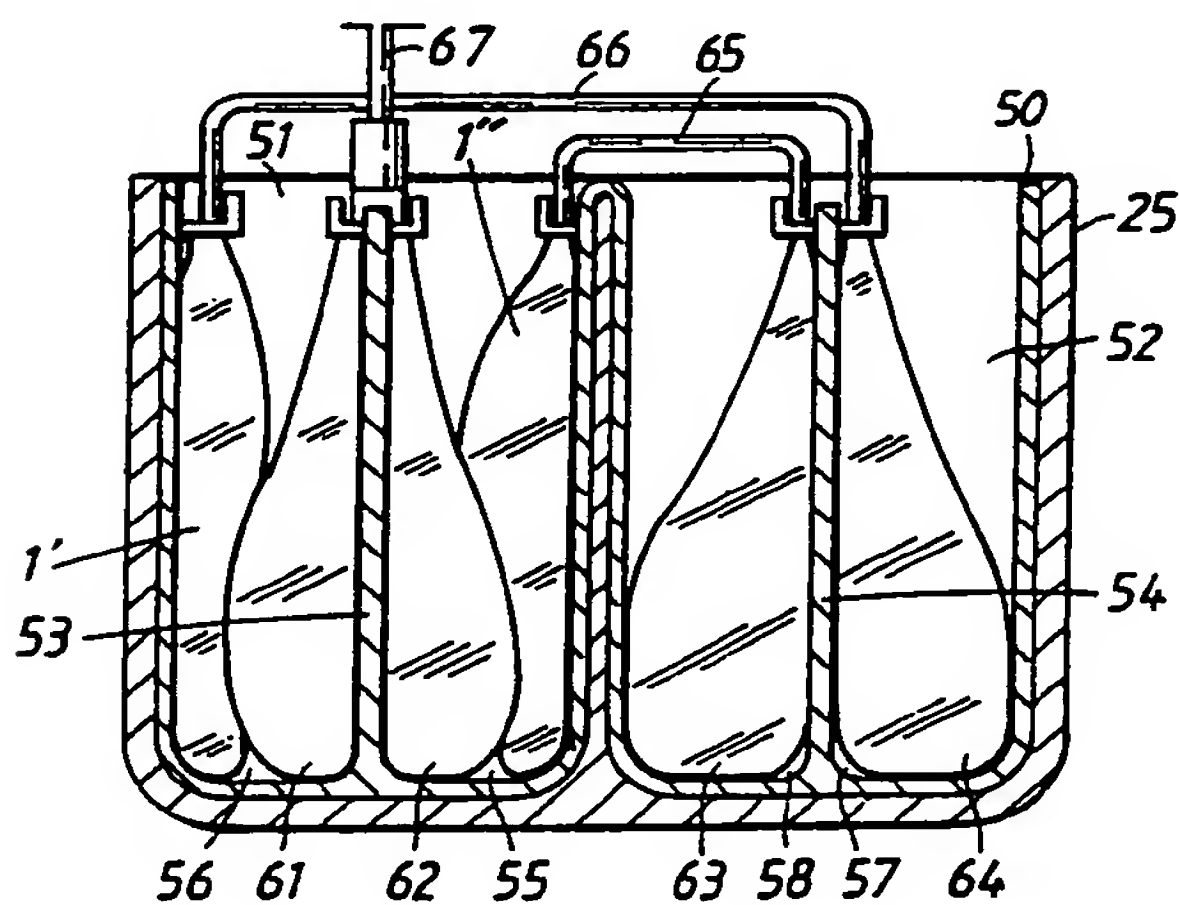


Fig. 7



SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International Application No **PCT/SE 91/00463**

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: B 04 B 5/04																	
II. FIELDS SEARCHED <div style="text-align: right; margin-right: 100px;">Minimum Documentation Searched⁷</div> <table style="width: 100%; border: none;"> <tr> <td style="width: 20%; border: none; padding: 5px;">Classification System</td> <td style="border: none; padding: 5px;">Classification Symbols</td> </tr> <tr> <td style="border: none; padding: 5px; height: 40px; vertical-align: bottom;">IPC5</td> <td style="border: none; padding: 5px; vertical-align: bottom;">B 04 B</td> </tr> </table> <div style="text-align: center; margin-top: 10px; font-size: small;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched⁸</div> <p style="margin-top: 20px;">SE,DK,FI,NO classes as above</p>			Classification System	Classification Symbols	IPC5	B 04 B											
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IPC5	B 04 B																
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹ <table border="1" style="width: 100%; border-collapse: collapse; font-size: small;"> <thead> <tr> <th style="width: 10%;">Category *</th> <th style="width: 60%;">Citation of Document,¹¹ with indication, where appropriate, of the relevant passages¹²</th> <th style="width: 30%;">Relevant to Claim No.¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top;">X Y</td> <td style="vertical-align: top;">US, A, 4447220 (EBERLE) 8 May 1984, see abstract; figures 1,2,7 <div style="text-align: center;">--</div></td> <td style="vertical-align: top;">1,10,15, 16 9</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td style="vertical-align: top;">US, A, 4303193 (LATHAM, JR.) 1 December 1981, see figures 3-8,10 <div style="text-align: center;">--</div></td> <td style="vertical-align: top;">1,2,10, 11,12, 15</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">Y A</td> <td style="vertical-align: top;">US, A, 3211368 (J.J. SHANLEY) 12 October 1965, see figures 1-5; claims 6,13 <div style="text-align: center;">--</div></td> <td style="vertical-align: top;">9 1-16</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">A</td> <td style="vertical-align: top;">WO, A1, 8706857 (OMEGA MEDICINTEKNIK AB) 19 November 1987, see abstract <div style="text-align: center;">--</div></td> <td style="vertical-align: top;">1,10</td> </tr> </tbody> </table>			Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	X Y	US, A, 4447220 (EBERLE) 8 May 1984, see abstract; figures 1,2,7 <div style="text-align: center;">--</div>	1,10,15, 16 9	X	US, A, 4303193 (LATHAM, JR.) 1 December 1981, see figures 3-8,10 <div style="text-align: center;">--</div>	1,2,10, 11,12, 15	Y A	US, A, 3211368 (J.J. SHANLEY) 12 October 1965, see figures 1-5; claims 6,13 <div style="text-align: center;">--</div>	9 1-16	A	WO, A1, 8706857 (OMEGA MEDICINTEKNIK AB) 19 November 1987, see abstract <div style="text-align: center;">--</div>	1,10
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A	WO, A1, 8706857 (OMEGA MEDICINTEKNIK AB) 19 November 1987, see abstract <div style="text-align: center;">--</div>	1,10															
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>																	
IV. CERTIFICATION <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; padding: 5px;"> <div style="border: 1px solid black; padding: 5px; margin-bottom: 5px;"> Date of the Actual Completion of the International Search <div style="text-align: center; margin-top: 10px;">8th October 1991</div> </div> <div style="border: 1px solid black; padding: 5px;"> International Searching Authority <div style="text-align: center; margin-top: 10px;">SWEDISH PATENT OFFICE</div> </div> </td> <td style="width: 50%; border: none; padding: 5px;"> <div style="border: 1px solid black; padding: 5px; margin-bottom: 5px;"> Date of Mailing of this International Search Report <div style="text-align: center; margin-top: 10px;">1991 -10- 14</div> </div> <div style="border: 1px solid black; padding: 5px;"> Signature of Authorized Officer <div style="text-align: center; margin-top: 10px;"> Asa Fransson </div> </div> </td> </tr> </table>			<div style="border: 1px solid black; padding: 5px; margin-bottom: 5px;"> Date of the Actual Completion of the International Search <div style="text-align: center; margin-top: 10px;">8th October 1991</div> </div> <div style="border: 1px solid black; padding: 5px;"> International Searching Authority <div style="text-align: center; margin-top: 10px;">SWEDISH PATENT OFFICE</div> </div>	<div style="border: 1px solid black; padding: 5px; margin-bottom: 5px;"> Date of Mailing of this International Search Report <div style="text-align: center; margin-top: 10px;">1991 -10- 14</div> </div> <div style="border: 1px solid black; padding: 5px;"> Signature of Authorized Officer <div style="text-align: center; margin-top: 10px;"> Asa Fransson </div> </div>													
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
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A	US, A, 4322298 (PERSIDSKY) 30 March 1982, see abstract; figures 1-21 --	1-16
A	US, A, 3559880 (NAITO ET AL) 2 February 1971, see abstract; figures 2,3,10,12 -- -----	1,10

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
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		SE-B-C- 459791	89-08-07
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